DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/7/11 has been entered.

Claims 13-27, 36-48, 67, 75-103 are pending in the case.

Claims 13-27, 36-48, 67 are withdrawn.

Receipt of Information Disclosure Statements on 3/7/11 and 5/5/11, 5/19/11 is acknowledged.

Any rejection of record in the previous action not addressed in this office action is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 75-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunn et al. (US 6,248,569) in view of Thach (US Patent 5,342,782), Kappelman et al.

(Gene, 160, 1995, 55-98) (cited by applicant), Uberlacker et al. (Mol. Breeding, 2, 293-295, 1996), New England Biolab catalog.

Dunn et al. teach a vector comprising a site for a first restriction site that generates a 3'TA overhang (i.e. PacI) which is 5' to a site for a second restriction enzyme which generates blunt ends, (i.e. HpaI), and a promoter positioned 5' of the first site (See Fig. 2), such that DNA comprising an open reading frame inserted between the first and second site would have a 1 in three chance of being in frame with the open reading frame upstream of the first restriction site. (Dunn et al. also discloses a vector (Fig. 1A, 1B) comprising a first site for PacI, with sites for blunt cutters such as ScaI and NruI 3' of said site, with a promoter positioned 5' to the first site).

Thach teach that in order to obtain expression of an open reading frame of interest, it is placed in-frame downstream of a promoter in a vector teaches that one may adjust the sequence of an open reading frame such that it is in frame with a promoter upstream of the sequence, so that the correct reading frame is generated for the resultant protein (see col. 4, lines 36-65). It would have been obvious to one of ordinary skill in the art to have altered any out of frame sequence inserted in the vector of Dunn et al., in order to obtain the correct reading frame, as taught by Thach. The insertion of a sequence of interest into unique sites in a vector, using convenient sites, for expression of said sequence from a promoter on the vector, is a very well known method in the art, and such vectors are extremely well known and would have been obvious to one of ordinary skill in the art.

Kappelman et al. disclose the restriction enzyme SgfI, which leaves 3'TA ends, and its 8 bp recognition site, and its usefulness for genome analysis (see abstract, see page 55).

New England Biolabs teaches recognition sites for restriction enzymes, including those used in the claimed vector, including PmeI, EcoIICRI, SgfI.

Uberlacker et al. disclose that it is advisable to use vectors containing 8 bp recognition enzyme sites, in order to clone complete genes, since such sites would be rare in a genome of interest and therefore less likely to interrupt a gene of interest (see page 293).

It would have been obvious to one of ordinary skill in the art to have altered any out of frame sequence inserted in the vector of Dunn et al., in order to obtain the correct reading frame, as taught by Thach. The insertion of a sequence of interest into unique sites in a vector, using convenient sites, for expression of said sequence from a promoter on the vector, is a very well known method in the art, and such vectors are extremely well known and would have been obvious to one of ordinary skill in the art. It also would have been obvious to one of ordinary skill in the art to have inserted a well known site such as SgfI in the vector of Dunn et al. in view of Thach, since the use of any particular restriction enzyme site in a vector is well known in the art, and since the placement of known and useful restriction sites, such as SgfI, in any vector, for manipulation of DNA, was extremely well known in the art. The placement of SgfI in a vector would result in well known sequences when joined to a DNA of interest, and when treated with restriction enzymes whose recognition sites, and cleavage sites, were

well known in the art. One would have been motivated by the teaching of Uberlacker et al., which teaches the insertion of 8bp restriction sites in cloning vectors, since such sites are not likely to be present within an open reading frame to be expressed. In the absence of evidence to the contrary, the placement of any particular 8 bp recognition restriction site, in any vector or DNA sequence, would have been obvious to one of ordinary skill in the art. Restriction enzymes, their recognition sites, the nucleotides overhangs that they leave, and the sequences that are formed when DNA treated with said enzymes is joined with a particular DNA of interest, were well known, as was the manipulation of DNA using known and useful restriction enzymes, including inserting sequences encoding any restriction site, at any region of any DNA molecule. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicant's response filed 3/7/11 has been considered but has not been found convincing. Applicant has argued that more than 3,000 type II restriction enzymes have been described and that there was "it is thus highly unlikely that one of skill in the art would have honed in on these particular restriction enzymes, among the thousands available, for use with the vector of claim 75. Yet the Examiner has not pointed to any reason why one of ordinary skill in the art would select SgfI with PmeI or EcoICRI for use with the claimed vectors, nor is any such motivation present in the cited references, Accordingly, Applicants respectfully submit that a prima facie case of obviousness has not been established." Applicants further state that even if a prima facie case were

established, the declaration of Dr. Michael Slater provides that the claimed vectors work unexpectedly well in facilitating cloning without the need to purify the DNA fragment of interest.

Regarding the obviousness, it is maintained that the use of 8 cutter (i.e. rare restriction sites) in vectors, for cloning genes, was well known in the art, since it was taught that using such sites was preferred since rare sites would be expected to be infrequent in a gene of interest (see Uberlacker et al.). 8 cutter restriction sites such as SgfI and PmeI and EcoICRI are known in the art, as taught by the references.

The Declaration under 37 CFR 1.132 filed 3/7/11 is insufficient to overcome the rejection of claims 75-103 based upon Dunn et al. (US 6,248,569) in view of Thach (US Patent 5,342,782), Kappelman et al. (Gene, 160, 1995, 55-98) (cited by applicant), New England Biolab catalog as set forth in the last Office action because:

The Declaration states "data showing the percent efficiencies achieved using vectors according to the claimed invention which efficiencies were achieved without purifying the DNA fragment of interest. Random ligation of the restriction fragments present in the ligation mixture would provide an expected transfer frequency of the DNA fragment of interest of approximately 50%. Instead , we observed transfer frequencies, yielding vectors carrying the DNA fragment of interest, above 80% or even 95%. The cloning efficiencies achieved are surprising, and much higher than would be expected with this type of cloning". However, the data disclosed in the Declaration does not appear to have any comparison to any sort of control vector, showing that levels of cloning efficiency are the result of the particular restriction enzyme sites, i.e. SgfI, and

PmeI or EcoICRI . Although applicants argue that higher than expected frequencies are achieved, this is an assertion that is not supported by any evidence. It is not clear whether these particular enzyme sites are responsible for any increased frequency of cloning. Therefore, the Declaration is not found convincing.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Arden Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/

Primary Examiner, Art Unit 1636

NV
6/14/11